Normal range of ATPase and ATP synthesis rates of human skeletal muscle determined noninvasively by a QUantitative Energetic Stress Test

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Human skeletal muscle is well known to be composed of a heterogeneous population of muscle fibers with respect to ATPase activity, aerobic capacity, and fatigue resistance. Further, significant heterogeneity between fiber-types has been demonstrated in the resting metabolic profile of other mammalian skeletal muscles. In addition, human voluntary contractions follow an orderly recruitment of motor units. The degree of spacial recruitment during steady-state voluntary contractions will be correlated to the extent of neuromuscular fatigue developing in the initially activated motor units. These issues complicate the in vivo study of human skeletal muscle energetics.

The evaluation of chemical energetics in skeletal muscle has been significantly advanced within the last decade largely because of applications of ^{31}P magnetic resonance spectroscopy (MRS) techniques (Arnold,Matthews, & Radda, 1984; Chance,Leigh,Clark,Maris,Kent,Nioka, et al., 1986). The QUantitative Energetic Stress Test (QUEST) recently developed for the evaluation of human skeletal muscle was designed to i) measure separately ATP utilization from ATP synthesis, ii) control cytosolic conditions with respect to pH, and iii) minimize the variabilities associated with normal physiologic motor unit recruitment and fatigue development upon the measure (Blei,Kushmerick,Esselman, & Odderson, 1991).

Methods

Percutaneous, supramaximal twitch stimulation (1 Hz) of the median and ulnar nerves was applied in combination with ischemia to the finger and wrist flexors in 8 normal subjects during 3 repeated measures. The experiments utilized a 2.0 Tesla General Electric CSI spectrometer with continuous ^{31}P Magnetic Resonance Spectroscopy (MRS) acquisition. The protocol and data acquizition have been previously described (Blei et al., 1991). The sequential spectrum were analized using a least squares comparison with a high signal-to-noise spectrum referenced to a quantified fully-relaxed spectrum.

Results

The duration of the ischemia (360 sec) preceding the ischemic stimulation was sufficient to deplete the muscle oxygen stores. During the 1 Hz stimulation train, the mean initial rate of phosphocreatine (PCr) breakdown was 0.40% baseline [PCr]/sec ($\pm$ 0.07%/sec SD). The mean relative standard deviation of 3 repeated measures for an individual was 9%. The mean initial rate of depletion during stimulation significantly differed among subjects (ANOVA, $P<0.0003$) with a range of 1.7 fold. Small changes in pH were recorded, yet the mean pH did not exceed the range of 7.07 to 6.95 during the experiments. After a brief time delay, the recovery process approximated a monoexponential time course; however, the maximum PCr/(PCr + Pi) significantly overshot (93.7% $\pm$ 3.5% SD) the pre-stimulation control level (88.9% $\pm$ 2.3% SD; $P<0.0001$, paired t-test, n=24). The recovery time constant averaged 59.8 sec ($\pm$ 13.7 sec SD) for the eight subjects with a mean relative standard deviation of 3 repeated measurements for an individual of 9%. The mean recovery time constants significantly differed among the eight subjects (ANOVA, $P<0.0001$) with a range of 1.9 fold.

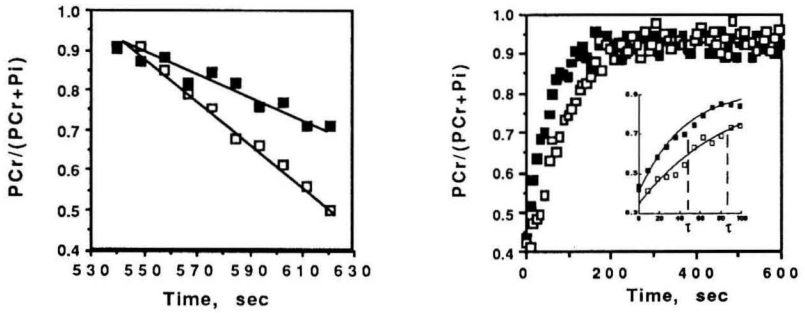

Figure 1. A) Range of initial rates of ATP utilization, and B) Range of recovery time constants in the eight normal subjects.

Discussion

The experimental protocol is able to achieve reproducible, independent, quantitative measures of high energy phosphate utilization and synthesis in human skeletal muscle. With respect to each energetic characteristic, it is capable of making statistical distinctions between individuals

The results demonstrate a predicted degree of intersubject variation. The human vastus lateralis has been previously shown to have a similar fiber-type distribution as the forearm flexors (Johnson,Polgar,Weightman, & Appleton, 1973). Utilizing biopsy data from the human vastus lateralis, the estimated range of energy utilization would vary 1.7 fold assuming simply a constant [PCr] among fiber-types and two fiber populations varying between 30-70% ST with a five fold difference in ATPase activity (Bárány, 1967; Chase & Kushmerick, 1988; Howald,Hoppeler,Claassen,Mathieu, & Straub, 1985; Johnson et al., 1973). Mitochondrial volume density in the vastus lateralis ranges from 4-7% or 1.75 fold. (Howald et al., 1985). These closely estimate the intersubject variability seen in our utilization data (1.7 fold) and recovery data (1.9 fold). In addition, the correlation between the calculated mean relative ATP utilization rates and synthesis time constants is: $r = 0.45$, $p<.05$, $n=8$; whereas, in Howald's data the correlation between fiber-types and mitochondrial volume density was: $r = 0.42$, $n=10$ (unpublished results). These results demonstrate the power of QUEST as a non-invasive biopsy of skeletal muscle composition and its potential in the serial monitoring of adaptation during specific training regimens and during pathological interventions.

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